

depletion of NOS substrates and co-factor.

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STN

TI Disruption of Rho signaling results in progressive atrioventricular
conduction defects while ventricular function remains preserved

AU Wei L (Reprint); Taffet G E; Khoury D S; Bo J; Li Y; Yatani A; Delaughter
M C; Klevitsky R; Hewett T E; Robbins J; Michael L H; Schneider M D;
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SO FASEB JOURNAL, (MAR 2004) Vol. 18, No. 3, pp. 857-+.
ISSN: 0892-6638.

PY 2004

AB Recent studies suggest that RhoA and Rac1 mediate hypertrophic
signals in cardiac myocyte hypertrophy. However, effects on cardiac
function caused by inhibition of their activity in the heart have yet to
be evaluated. Cardiac-specific inhibition of Rho family protein
activities was achieved by expressing Rho GDIalpha, an endogenous specific
GDP dissociation inhibitor for Rho family proteins, using the alpha-myosin
heavy-chain promoter. Increased expression of Rho GDIα led to atrial
arrhythmias and mild ventricular hypertrophy in adult mice (4-7 months).
However, left ventricular systolic and diastolic function was largely
preserved before and after the development of cardiac hypertrophy,
indicating that Rho GTPases are not required to maintain ventricular
contractile function under basal physiological condition.
Electrocardiography and intracardiac electrophysiological studies revealed
first-degree atrioventricular (AV) block in the transgenic heart at 1 week
of age, which further progressed into second-degree AV block at 4 weeks of
age before the development of cardiac hypertrophy. Expression of
connexin 40 dramatically decreased from 1 week to 4
weeks of age in the transgenic heart, which may contribute in
part to the conduction defects in the transgenic mice. This
study provides novel evidence for an important role of Rho GTPases in
regulating AV conduction.

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L1 327 S CONNEXIN 40 OR CXN40
L2 68613 S TRANSGENIC
L3 2 S L1 (S) L2

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L4 12 S L3

FILE 'PCTFULL' ENTERED AT 12:27:23 ON 24 JAN 2008

L5 0 S L3

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L6 3 S L3

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